A Dissertation on

Aggressive Fibromatosis – Government Royapettah Hospital Experience

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BONAFIDE CERTIFICATE

This is to Certify that **Dr. P.Saravanan,** bonafide student of M.Ch. Surgical Oncology. (July 2007 to August 2010) in the Department of Surgical Oncology, Government Royapettah Hospital, Chennai – 600 014 has done this dissertation on "**Aggressive Fibromatosis-Govt Royapettah Hospital experience"** under my guidance and supervision in partial fulfilment of the regulations laid down by The Tamilnadu Dr.M.G.R. Medical University, Chennai for M.Ch. Surgical Oncology Examination to be held in August 2010.

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CONTENTS

Aim of the study

1. To study the epidemiological characteristics of the disease in India
2. To analyze the surgical data and present the outcome.
3. Describe the pattern of recurrence and salvage modality for recurrence.
4. To find out the optimal management strategy for this rare disease

Introduction

Aggressive Fibromatosis also known as Desmoid tumors is a monoclonal disorder affecting the musculoaponeurotic tissues. It is relatively a rare neoplasm with a frequency of about <3% of all soft tissue tumors and annual incidence of about 0.2 to 0.5 per 100000 population. Exact etiology of aggressive fibromatosis is currently unknown. It is probably multifactorial with hormonal, genetic and trauma playing their parts. They are locally infiltrative and never metastasize but have a tendency for multiple recurrences. The morbidity caused by this lesion is due to local destruction of tissues and occasional death has been reported[(2)].

Aggressive Fibromatosis are heterogenous group of tumors which share similar clinical, histological and molecular genetic feature. But each type has some subtle and unique feature which distinguishes it from others. Due to the relative rarity of this tumor and their enigmatic clinical behavior, treatment for fibromatosis has not been

optimized. In this article we will be discussing about our experience with deep fibromatosis.

Materials and methods

A retrospective analysis of our data over a period of 13 yrs (between 1998 and 2010) was done. There were 33 patients with a diagnosis of deep fibromatosis in our records which included abdominal, intra-abdominal and extra abdominal. In 28 patients a wide excision of the lesion was performed with curative intent. Adjuvant radiotherapy was given for 4 patients and systemic therapy in the form of tamoxifen was given for 4 patients.

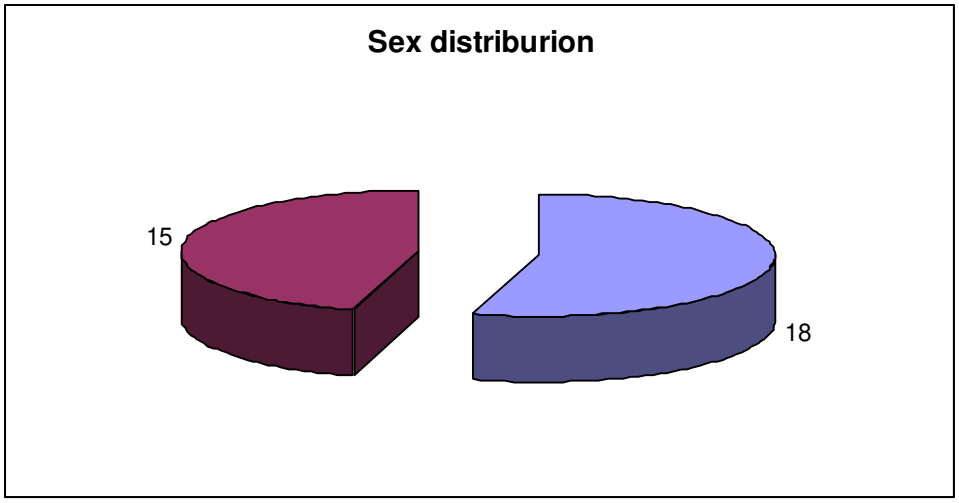
Information regarding epidemiological characteristics of the disease, surgical procedure performed postoperative margin status on histopathological examination, adjuvant treatment given, recurrences in the follow-up period, pattern of recurrence and salvage modality for recurrence were collected for analysis.

Observation and Analysis

The disease and its natural course to some extent were described 170 years ago. Although numerous researchers have dedicated their time to acquire more knowledge about this disease, every aspect of this disease beginning form etiology to management is full of controversies. The enigma of fibromatosis will continue to haunt the researchers for some more time as new findings (like ERβ) lead to more questions than answering the older ones. In this analysis we will concentrate on the Indian perspective about the disease and explore the lacunae in the literature.

Demographic trend

There were 18 female patients & 15 male patients a ratio of around 1.2:1. In western literature a female preponderance in the ratio of 3:1 is described. In pediatric age group fibromatosis is extremely rare and has a male preponderance. We had 5(15%) pediatric patients and 4 of them were male.



The mean age of presentation is 25.8, ranging from 7 to 64. The number of swelling at presentation ranged from one to 6. The size of the tumor ranged from 3cms to 20cms, mean 9cms. There were 21 primary tumors and 12 recurrent tumors. The average duration of presenting symptom was more with recurrent tumors than with primary tumors.

Enzeinger & Weiss's classification which is widely accepted is utilized for classifying deep fibromatosis in this article.

Table 1. ***Deep(Musculoaponeurotic) Fibromatosis - Enzeinger & Weiss***

Extra- abdominal fibromatosis	28
Abdominal fibromatosis	1

Intra - Abdominal fibromatosis

Pelvic fibromatosis	1
Mesentric fibromatosis	3
Mesentric fibromatosis in Gardner syndrome	0

Table 2. ***Site distribution of Extra abdominal fibromatosis***

Shoulder	3
Arm	9
Fore arm	2
Gluteal	2
Thigh	5
Leg & foot	3
Head & Neck	2
Lower limb	2

Fibromatosis has a predilection to affect muscles around the shoulder and pelvic gridle followed by other locations. In our series, there were 12 tumors around the shoulder gridle and 9 around the pelvic gridle. Site distribution in our series is in concordance with western literature except there were no cases associated with Gardners syndrome, which is rare in India.

Demographic pattern of the disease in our series with regards to age range, location & site distribution is in concordance with the

western literature. But there is an increased male sex and pediatric age group incidence in our series. We could not find any reason for this increased incidence. Whether this constitutes a different demographic trend in India for this disease can be confirmed only when data from different parts of the country is pooled and analyzed. Although only one patient was diagnosed to have abdominal fibromatosis, we believe the incidence to be more. The lower incidence might be due to different referral patterns than due to real difference the demographic trend.

Management

We discuss all our cases in multidisciplinary tumor board & offer surgical excision as primary treatment for operable tumors and radiation or systemic therapy for inoperable tumors. In few of these patients histology can be inconclusive since fibromatosis contains few neoplastic cells and more collagen. In such cases a decision to operate is taken after considering the clinical and imaging findings.

26 patients with extra abdominal fibromatosis, 1 with abdominal and 1 with mesenteric fibromatosis underwent surgery. 2 mesenteric, 1 head & neck and 1 pelvic fibromatosis were inoperable

due to extensive local infiltration. 2 patients refused any form of therapy.

The details of 26 patients with extremity, 1 with abdominal and 1 with mesenteric fibromatosis who had undergone primary surgical excision are given in

table 3.

Table 3.*Details of patients who had under gone surgery for Aggressive fibromatosis in our department*

Age	
Range	7 – 42
Median	30
Sex	
Male	12
Female	16
Mean Size	9.5 cm
Site	
Shoulder	3

Arm	9
Forearm & Hand	2
Gluteal	2
Thigh	5
Leg & Foot	3
Anterior abd wall	1
Head & Neck	1
Mesentric	1
Lower limb	1
Presentation	
Primary	17
Recurrent	11

The mean tumor size in the surgical group was 9.5cms. In all but one patient limb salvage was done successfully. One patient who had undergone limb salvage surgery along with vascular resection has to be amputated as she developed vascular graft infection. Surgical excision constituted a wide monobloc excision with 1cm margin. Clearance near vital structures was conservative to preserve maximum function. All oncological principles followed in limb salvage surgeries done for sarcomas were adhered to. Surgical procedure ranged from wide excision of the tumor to complex muscle group excision. Details of the limb salvage procedures undertaken are given in table 4.

Table 4: Details of the surgical procedure

Surgical procedure	**No of patients**
Wide monobloc excision	19
Scapulectomy	3
Centralisation of Ulna	2
Excision of metatarsals with bone grafting	2
Laparotomy and excision	1
Amputation	1

<u>Abdominal Fibromatosis- Paucity of data</u>

Only one of our patients had abdominal fibromatosis. This patient was quite young (14 yrs) and was not associated with pregnancy. She was treated with wide excision and no adjuvant was given. She is disease free till now. This fact is surprising as abdominal fibromatosis has much higher incidence than what is seen in our series. This might be due to different referral patterns than due to real difference the demographic trend.

Intra abdominal fibromatosis - Hig risk site for inoperability

In our series there were 4 patients who had intra abdominal fibromatosis - 2 mesentric, 1 retroperitoneal and 1 pelvic. In only one of these patients we were able to achieve complete surgical excision. This reiterates the fact that intraabdominal fibromatosis is high risk region for inoperability. But surgical exploration with intent to completely excise the tumor should be the aim since it is associated with long term local control. One of our patients with retroperitoneal fibromatosis in whom a complete excision was possible is disease free until now although no adjuvant was given to him. 1 patient with mesenteric fibromatosis who was put on tamoxifen after finding his disease inoperable is having a stable disease for the past 5 years.

Recurrences and pattern of recurrence

We experienced 12 recurrences (40% recurrence rate) in our series. All recurrences were salvaged by revision surgery. Various variables taken up for analysis of recurrences are given in table 5.

Table 5. Comparison between recurrent and disease free group

	Disease free group	**Recurrence group**	**Time taken to recur**
No Patients	22	6	
Site	Not siginificant	Not siginificant	
Size	9cm	9.5cm	
Median Age	29	35	
Number of primary tumor			
Single	19	4	16 months
Multiple	3	2	13 months
Status of margin			
Positive	2	4	15 months
Negative	20	2	11 months
Presentation			
Primary	15	2	13 months
Recurrent	7	4	16 months

In the surgical group there were 5 positive margins and 1 close margin. Median follow-up time in our series is 5 yrs. There were 12 recurrences in the surgical group an incidence of 40%. All our recurrences were salvaged by revision surgery. 4 patients were offered adjuvant radiation. All inoperable tumors were offered tamoxifen.

In our series sex, site of the tumor, multiplicity of the tumor at presentation or size of the tumor did not influence recurrence. Presentation - primary vs recurrent was associated with increased recurrence rate, 24% of primary & 56% of recurrent tumors experienced recurrence. Status of the margin, positive vs negative had a positive impact on recurrence, 10% in disease free group and 66% in recurrent group had positive margins.

The propensity of aggressive fibromatosis to locally recur is related to its infiltrative nature, which makes it difficult for the surgeon to grossly identify the true extent of disease. These tumors lack a pseudocapsule and display nonpalpable diffusion along muscle bundles and fascial planes. This may justify the high recurrence rate of the disease after adequate surgery. Posner et al, Goy et al and Spear et al

identified positive resection margins as the most important Independent predictive factor of local recurrence. But in a study by Merchant et al and in few other studies positive margin does not affect the outcome adversely. Gronchi et al speculates that the recurrence rate highly depends on inherent characteristics of the disease, which might be more or less aggressive on its own, so that it might recur or not rather independent of the fine quality of surgery.

In Gronchi et al's series, patients with large tumors located at the extremities or girdles had a higher risk of recurrence, regardless of whether they were excised with positive or negative resection margins. We did not find any such association between site and recurrence.

The most intriguing aspect of our recurrence pattern is the time to recur. Although positive margin in our series was associated with high recurrence rate, the duration taken for the tumor to recur in both the positive margin group and negative margin group did not show any significant difference. The number of tumor at presentation, single vs multiple and the presentation, primary vs recurrent, also did not show any significant difference in the time taken to recur.

Although we could not find any literature evidence to support this fact, we believe this fact reiterates that recurrences in fibromatosis may be more influenced by the biology of the disease.

Pattern of recurrence in fibromatosis can also be quiet different from other tumors. Recurrences can be within the surgical field or also away from it. In our series one patient who had a tumor in the origin of coracho brachialis after surgical excision experienced recurrence at lower end of the muscle about 10 cm away from the primary tumor and another recurrence in pectoralis major muscle. Whether this is due to intra muscular microscopic infiltration of the tumor along the muscle spindles or a genetic field defect in the affected muscles is unknown. In few patients the recurrences can be just outside the radiation field. One of our patients experienced a recurrence just outside the radiation field.

Adjuvant therapy

4 of our patients received adjuvant RT out of which 1 experienced recurrence which was salvageable by revision surgery. Recommendations for adjuvant radiation have not been standardized. As most of our patients are young and all our recurrences are salvageable by revision surgery we do not offer adjuvant RT routinely to avoid long term complications of RT. We recommend it for multiple recurrences, positive margin and multiple tumors at presentation to avoid mutilating salvage surgery.

We offer Tamoxifen to all inoperable tumors. One of our patients with mesenteric fibromatosis is having stable disease for the past 5 years. We could not come to any conclusion on the efficacy of tamoxifen since all other patients are lost to follow-up. We also offer tamoxifen in adjuvant setting for patients who had experienced multiple recurrences. The efficacy of tamoxifen in adjuvant setting could not be analysed in our patients as the number is very small. We are yet to find a clinical situation in which cytotoxic chemotherapy is to be considered.

Multicentric Fibromatosis – Describing a new entity

Fong et al has described an entity where multiple lesions are found typically confined to one anatomical region of the body. In most cases the second growth is found proximal to the first growth. This is found in 5% of the patients diagnosed to have extra abdominal fibromatosis.

Although multicentric fibromatosis confined to one anatomical region is a known entity, we describe a new hitherto undescribed non random pattern of distribution of multicentric extremity fibromatosis.

Two male patients presented with multiple fibromatosis of lower limb distributed in gluteus muscles, quadriceps, muscles of popliteal fossa and a lesion in between metatarsals in the foot. One patient underwent wide excision of all lesion and is disease free for the past one year. The other patient, who has had the disease for the past 10 years, refused any form of treatment. In both patients the tumors were around the hip and knee joint and both of them had the disease

for more than 10 years. Fong et al's observation of second growth arising proximal to the first one was not seen in both patients. The new lesions arose both proximal and distal to the index lesion.

One female patient had multiple lesions in the upper limb distributed along Pectoralis major, Biceps, Corachobrachialis and between the metacarpals. These tumors were found arising around the shoulder and knee joint and again the new lesions arose both proximal and distal to the index lesion.

In all the three patients the lesions were separated widely and found to cross the joints as well. This fact rules out the possibility of skip metastasis or a contiguous spread from the index lesion. The nonrandom pattern of distribution especially the tumors arising between the metacarpals and metatarsal is striking and is not possible with any known local infiltrative patterns.

We believe the muscle groups involved in this form of fibromatosis acquires a genetic defect and some other environmental or hormonal factor makes the tumors to manifests itself at a later age.

Since it does not affect the other limbs or other muscle groups of the body the environmental insult probably happens at the time of limb development. Molecular analysis of the involved muscles and adjacent muscles might shed more light in this matter.

Literature Review

Etiology and Genetics

Exact etiology of aggressive fibromatosis is currently unknown. It is probably multifactorial with hormonal, genetic and trauma playing their parts. Trauma as causative factor is controversial. Although there are many anecdotal reports suggesting trauma as an important causative factor it remains to be established. The long standing controversy regarding the nature of this lesion, whether neoplastic or reactive, appears to be answered with consistent cytogenetic abnormalities found in these tumors.46% of deep tumors and 10% of superficial tumors show trisomies 8 & 20 and loss of $5q^{(1,3)}$. These findings prove it to be a true neoplasm rather than a reactive lesion.

Beta catenin pathway

Sporadic as well as FAP associated fibromatosis show elevated levels of beta catenin levels. Mutations in APC gene leading to abnormal levels of beta catenin resulting in a growth advantage is the

central abnormality in most of these tumors. This pathway is known as WNT –APC-Beta –Catenin signaling cascade.

What ever may be the genetic abnormality it appears to remain stable through out the life, evident from the fact that sarcomas do not arise from fibromatosis even in patients with long standing disease. Beta catenin stabilizing mutations, apart from fibromatosis have been found in other benign conditions like Pilomatrixoma and Hepatoblastoma. This suggests that fibromatosis is essentially a benign condition although it mimicks malignancy in many ways.

Fibromatosis and Estrogen receptors

It is a well known fact that some of these tumors respond to Tamoxifen but estrogen receptor has been found only in few of these tumors. Immunohistochemical analyses have consistently shown these tumors to be negative for ERα and c- Kit. But this neoplasm does have an hormonal influence ,especially to estrogen . This is suggested by the following facts

1. Female preponderance,

2. Growth rate increases during pregnancy and

3. Anecdotal reports of complete regression of these tumors with Tamoxifen.

Recently in 1996 the presence of second estrogen receptor has been discovered and named as ERβ, the traditional receptor has been named ERα. Fibromatosis has shown to express more of ERβ and this explains the clinical efficacy of antiestrogens even in the absence of conventional estrogen receptor. Reports of this tumor responding to imatinib may not be due to c- kit mutations.

Clinical presentation

Classical presentation is a deep seated mass that is painless and slow growing. It may cause restriction of movements and can affect the bone as well. They are locally infiltrative and never metastasize but have a tendency for multiple recurrences. The morbidity caused by this lesion is due to local destruction of tissues by direct infiltration and pressure effects. Occasional death has been reported due to involvement and destruction of vital organs. No paraneoplastic

conditions have ever been described, fibromatosis coexist with the host peacefully.

Aggressive fibromatosis commonly affects shoulder followed by chest wall, back, thigh and head and neck. Fibromatosis of head and neck is particularly aggressive causing massive destruction of soft tissue and bone often resulting in fatal outcome.

Aggressive fibromatosis is more common in females, most authors report a male to female ratio of 3:1. However in children the sex incidence is equal. Desmoid tumors can occur during any age but they are extremely uncommon during the extremes of the age. Most common age group to be affected is between 10 and 40.

Histologically these lesions appear benign but have an aggressive clinical behaviour. Characteristic microscopic finding are abundant collagen with uniform appearing spindle shaped cells which are widely distributed and have little or no cell to cell contact. Mitoses are few in number. At the periphery the tumor infiltrates into surrounding musculature.

Classification

Reitamo et al classified these tumors into 4 major clinical groups

1. **Juvenile** – Extra abdominal location with a predilection for young girls of less than 15 years.
2. **Fertile** – Abdominal in fertile females
3. **Menopausal** – Abdominal but with equal male and female incidence
4. **Senescent** – Both abdominal and extra abdominal with equal sex distribution

Recently Enzinger has classified these tumors more comprehensively into two major groups superficial and deep (Table 1).

Table 1

Superficial(fascial)Fibromatosis

Palmar fibromatosis(Dupuytren's disease)

Plantar fibromatosis(Ledderhose'disease)

Penile fibromatosis(Peyronie's disease)

Knuckle pads

Deep(Musculoaponeurotic) Fibromatosis

Extra- abdominal fibromatosis

Abdominal fibromatosis

Intra abdominal fibromatosis

Pelvic fibromatosis

Mesentric fibromatosis

Mesentric fibromatosis in Gardners syndrome

Superficial fibromatosis arise from fascia and aponeurosis , are slow growing and small. They rarely involve the deep structures. The

natural course of disease have two phases, first is a cellular proliferative phase followed by a late collagenous contractile phase. Deep fibromatosis are rapidly growing tumor and often attain a large size. Their biological behavior is aggressive compared to superficial fibromatosis. The natural course of fibromatosis is still an enigma. The disease manifestation ranges from spontaneous regression in some patients to multiple recurrences in some. Some authors have described a stable phase for the disease during which the size of the tumor does not change, this period ranges from 6 months to 3 years.

Extra abdominal fibromatosis

Extra abdominalfibromatosis is synonymous with aggressive fibromatosis, desmoid tumor and extra abdominal desmoid tumor[(4)]. It arises from connective tissue of muscle and the overlying fascia and aponeurosis. It is most common in patients between puberty and 40 years of age. 5% of the patients are below 10 yrs of age. Common clinical presentation is a painless deep seated mass. Decreased mobility of the affected joint may occur.

Aggressive fibromatosis affected patients have multiple minor bony abnormalities. This may be present in upto 80% of patients. This

includes cortical thickening, exostoses and areas of cystic translucence or compact islands in the femur(or both).

In the shoulder and neck region it most commonly affects the deltoid,scapular region,supraclavicular and posterior cervical triangle from where it may descend into anterior or posterior portion of the axilla and arm.

Fibromatosis of the pelvic gridle primarily affects the gluteus muscle, in the thigh it affects quadriceps and muscles of popliteal fossa. Hand and foot are rarely affected.

Although Enzinger & Weiss has grouped extra abdominal fibromatosis under one umbrella there may be different sub groups with distinct clinical behavior. Two of them are Head & Neck fibromatosis and Pediatric fibromatosis.

Pediatric fibromatosis

The overall incidence of AF in childhood is estimated at 2–4 new diagnoses per 1 million per year. Childhood AF has an age distribution peak at approximately 8 years (range, 0–19 years) with a slight male

predominance.more than one third of them occur in head and neck region[6]. Surgery is the recommended treatment and the role of adjuvant therapies are yet to be standardized. Late toxicity and occurrence of second malignancy should be taken into consideration when prescribing adjuvant treatment.

Head and neck fibromatosis

Head and neck region is affected in upto 23% of patients with extraabdominal fibromatosis. It usually affects younger patients. The soft tissues of the neck are most commonly affected followed by oral cavity, scalp, paranasal sinuses and orbit. This subtype particularly aggressive and is capalble of producing massive destruction of adjacent bone and erosion of base of the skull[5]. They occasionally encroach trachea and may result in death.

Multicentric fibromatosis

Fong et al has described an entity where multiple lesions are found typically confined to one anatomical region of the body. In most cases the second growth is found proximal to the first growth. This is found in 5% of the patients diagnosed to have extra abdominal fibromatosis.

Rarely co existence of abdominal and extra abdominal fibromatosis has been found in the same patient.

Abdominal fibromatosis

Abdominbal fibromatosis occurs in young, gravid or parous women during gestation or more frequently during the first year following child birth[19,20&30]. The tumor arises from musculoaponeurotic structures of abdominal wall, especially rectus and internal oblique and their fascial coverings. There may be a solitary lesion or multiple lesions[8]. Endocrine etiology is strongly believed because of its frequent association with pregnancy and few reports of spontaneous regression with menopause. Wide local excision is the treatment of choice but multiple recurrences are common.

Intraabdominal fibromatosis

The intraabdominal fibromatosis includes a group of closely related lesions rather than single entity which have similar histology but distinct location and clinical behavior. They include Pelvic fibromatosis, Mesentric fibromatosis and fibromatosis of Gardners

syndrome. These tumors share similar clinical, histological and molecular genetic features but each type has some subtle and unique feature which distinguishes it from others.

Mesentric fibromatosis

Fibromatosis is the most common tumor of the mesentry and occounts for 8% of all fibromatoses. Most cases are sporadic but few are associated with FAP/Gardners syndrome. Small bowel mesentry is the most common location but it may affect iliocolic mesentry, gastrocolic ligament, omentum or retroperitoneum. Clinically it is difficult to distinguish it from retroperitoneal fibrosis and sclerosing mesenteritis. Other important differential diagnosis is GIST. Excision is the treatment of choice but is often difficult due to irregular growth and attachment to mesentry. Other alternatives like anti estrogens, cytotoxic chemotherapy and radiotherapy have been used with variable results.

Mesentric fibromatosis associated with Gardners syndrome

The incidence of desmoid tumors with poloposis coli is around 10 to 15%. It usually occurs 1 to 2 years after excision of disease portion of the colon. These lesions are the most common cause of

death in patients with polyposis coli after colectomy[7,9,10&11]. Treatment is similar to mesenteric fibromatosis without gardners syndrome but multiple recurrences are common.

Pelvic fibromatosis

Pelvic fibromatosis occurs in young females between 20 and 35 and often unrelated to gestation or child birth. They are present as slow growing painless pelvic masses. Clinically they mimic ovarian masses or mesenteric cyst. Large tumors encroach on urinary bladder,vagina or rectum. They may cause hydronephrosis. Surgical treatment is the standard one. A suprapubic approach alone or in combination with an inguinal approach is recommended. Hemipelvectomy may be required sometimes to achieve R0 resection, instead of this morbid procedure a conservative approach with tamoxifen and NSAIDs have been tried with some success.

Pathology

On gross examination, the tumours are always confined to the musculature and the overlying aponeurosis or fascia. Their size varies from 5 to 20 cm. The tumours are firm, cut with a gritty sensation, and on crosssection reveal a glistening white, coarsely trabeculated surface resembling scar tissue.

Microscopically, desmoid tumours are poorly circumscribed, infiltrating the surrounding tissue. The proliferation consists of elongated, slender, spindle-shaped cells of uniform appearance. The tumour cells are surrounded and separated from one another by abundant collagen, with little to no cell-to-cell contact. The cells lack atypia, but cellularity may vary within the same lesion. Nuclei are small, pale-staining, and sharply defined. One to three small nucleoli are usual.

Ultrastructurally, desmoid tumours consist of a uniform population of elongated fibroblast-like cells, often terminating in long, slender processes. Most nuclei are rounded or oval, but some cells show prominent nuclear indentations or clefts. There is a prominent

rough endoplasmic reticulum, partly dilated, containing granular or fibrillary material within the dilated spaces. The cytoplasm has a small number of mitochondria, a prominent Golgi apparatus, free ribosomes, and occasional pinocytotic vesicles and microtubules. Some cells contain intracytoplasmic

bundles of actin-type microfilaments, and incomplete or clumped basal lamina along the cell borders, all features characteristic of myofibroblasts. The stroma contains considerable amounts of collagen and ground substance.

Imaging of Desmoid Tumors

Radiographs may be normal or may show a nonspecific soft-tissue mass. Calcification is uncommon. Underlying bone involvement is seen in 6%–37% of patients, typically with pressure erosion and cortical scalloping but without invasion of the medullary canal .Bone scintigraphy usually demonstrates increased uptake on blood pool and static images. Angiograms are variable in appearance, often showing marked hypervascularity, although some lesions demonstrate no vascular blush.

CT scans of the deep fibromatoses are also usually nonspecific. Lesions may be hypoattenuating relative to skeletal muscle but are typically isoattenuating or even hyperattenuating. The latter finding may be related to lesions with more extensive collagen. Lesions usually demonstrate enhancement after intravenous administration of iodinated contrast material; the enhancement is sometimes marked[18]. Owing to the infiltrative growth pattern and the attenuation similar to that of skeletal muscle, the margins of the lesion are often indistinct at CT unless it is separated from normal tissue by a fat plane. Subtle pressure erosions of bone are often better evaluated on radiographs owing to beam-hardening artifact at CT.

The best imaging modality for evaluation and staging of the deep fibromatoses is MR imaging. Extraabdominal desmoid tumors are typically intermuscular lesions, although muscle invasion is common. In addition, linear extension along fascial planes is a frequent manifestation and is uncommon with other soft-tissue neoplasms. The MR imaging pattern of the deep fibromatoses has been highly variable. The most common signal intensity pattern is heterogeneous, with intermediate signal intensity (similar to that of fat on T2-weighted

images and similar to that of skeletal muscle on T1-weighted images) seen with standard pulse sequences .The heterogeneous signal intensity pattern likely corresponds to the varying proportions of cellular tissue, myxoid tissue (high water content and high signal intensity on T2-weighted images), and collagen (low signal intensity with all pulse sequences) in the lesion .Prominent low-signal-intensity bands are often seen with all pulse sequences and are likely related to the dense areas of collagen .Areas of low signal intensity with all pulse sequences are characteristic of fibromatosis but not specific for it. Other types of soft-tissue masses with prominent low signal intensity on T2-weighted images include giant cell tumor of tendon sheath (a localized form of pigmented villonodular synovitis), calcified masses, and malignancies such as fibrosarcoma or malignant fibrous histiocytoma .The deep fibromatoses typically demonstrate moderate to marked enhancement after administration of gadolinium contrast material, particularly in less collagenized and more cellular regions .Only 10% of lesions lack significant enhancement at MR imaging .Lesion margins at MR imaging may be well defined or infiltrative.

MR imaging should be used for preoperative staging, particularly to evaluate for neurovascular and bone involvement. In extremity lesions, the entire limb should be imaged to rule out multicentric disease. MR imaging is also the best imaging modality to evaluate for postsurgical local recurrence. Recurrent deep fibromatosis shows intrinsic MR imaging characteristics similar to those of the original lesion. The site of recurrence is frequently at the lesion margins at areas of fascial extension where surgical resection is incomplete, leaving residual tumor. In patients who undergo radiation therapy or chemotherapy alone without surgery, MR imaging is useful in evaluating the effectiveness of therapy. Effective therapy (good lesion response) is indicated by a reduction in size and an increasing degree of low signal intensity on T2-weighted images, which reflects increased collagenization in response to therapy.

Biopsy method

There have been only a few published studies of single cases or relatively smallseries of desmoids examined by FNA, with some indicating its usefulness (Raab et al. 1993, Åkerman 2003) and others pointing out the pitfalls of occasional misinterpretation of

malignancies (Powers et al. 1994, Dey et al. 2004). The occasional over-diagnosis of sarcoma in desmoid tumors using FNA and the under-recognition of sarcomas falsely diagnosed as desmoids on FNA is reported by Åkerman et al.

The few reports of core needle biopsies in the preoperative diagnosis of desmoids suggest that it is a very useful technique (Serpell and Pitcher 1998, Ray- Coquard et al. 2003). The simplicity of the core needle biopsy technique, the almost constant representative material obtained in the hands of surgeons or others with experience, the abundance of material obtained that allows recognition of the histological characteristics and growth pattern, and the high degree of diagnostic accuracy all suggest that this technique is the diagnostic method of choice. FNA still has a role to play in the diagnosis of desmoids, particularly in cases with tumors located at sites that are in close proximity to major vessels or nerves, pleura and lungs, which would lead to unnecessary risks or complications when a core needle biopsy is used.

Management

Treatment for fibromatosis has not been optimized. Goals of the management are to attain local control with maximum preservation of function and cosmesis. But what constitutes adequate treatment is still elusive. As of today surgery forms the main stay of treatment and radiation has been used in adjuvant setting and for inoperable tumors. Cytotoxic chemotherapy, NSAIDs and hormonal therapy has been used with varying success but the results are less predictable.

Surgery

Surgical treatment produces a local control of about 70% and an overall 5yr survival in excess of 90% in many series. Surgical treatment for this lesion has considerable controversies. Local recurrence after surgical resection alone ranges from 40% to 60% in most series[15&16]. Recurrences had been within the surgical field and also away from it. Some of the high risk factors associated with local recurrence are presentation – primary vs recurrent tumors and quality of surgical margin free vs close or positive. Positive surgical margin has been found to be a siginificant predictor of local recurrence in many series including that of Gronchi et al. But many other series have

found equal recurrence rate with positive as well as negative surgical margin. In few series a positive margin is a predictor of local failure for recurrent lesions but not for primary tumors. Extent of resection required for these lesions is yet to be standardized. Most authors recommend a wide surgical margin of about 1cm. The consensus is a close or positive margin while preserving the function is acceptable.

Radiation therapy

Radiation therapy alone or in addition to surgery has been reported to give superior local control rates in few series (Spear et al and Ballo et al). Nuyttens et al in a review of 22 articles comparing surgery and radiation found that local control rates were more with combination of surgery and radiation and radiation alone than for surgery alone. These authors recommended that mutilating surgeries should be avoided and more conservative approach should be chosen. But most of these reviews included only a few numbers of patients and patients were chosen for radiation therapy at the discretion of surgeon or radiation oncologist. Moreover these articles do not take into consideration about the stable phase of disease while measuring the response to treatmet. All these factors make most authors recommend

surgery as the primary treatment for operable tumors and radiation as adjuvant. Indication for adjuvant radiation has not been standardized though most authors would recommend it for recurrent tumors, margin positive tumors and multiple tumors[12,14,21,22,24&25]. Most series recommend a dose of about 50 to 60 Gy.

Systemic therapy

The role of cytotoxic, noncytotoxic and hormonal therapy has been reviewed recently by Jannis et al. There are no randomized control trials which have evaluated the role of various systemic therapies for fibromatosis but there are many case series reports on this subject[26,27,28,31,33,34&35] . Agents used as systemic therapy includes sulindac, tamoxifen, combination chemotherapy with methotrexate and vinblastine or doxorubicin based chemotherapy. Indication for systemic therapy are

1.To avoid mutilating surgery,

2.Inoperable mesenteric and retroperitoneal tumors and

3.Recurrent tumors.

Optimal duration of these treatments should be based on clinical benefit and tolerance.

To conclude surgery is the standard of care in managing fibromatosis, radiation is an useful adjuvant and medical management can be given a try before proceeding with mutilating surgey or amputation

Updates in the management of Desmoid tumors and our experience

Recently, many articles coming up describing a stable phase in the natural course of disease, ranging from 6 months to 36 months. After the stable phase, the tumor either increases or decreases in size. This will have a major impact on the treatment rendered and assessment of response to treatment in future.

Whether performing the surgery during the stable phase of the disease will reduce the recurrence is to be investigated. Exploring the possibility of inducing and maintaining the disease in stable phase through systemic therapy will have to be seen

Conclusion

Demographic trend in India might be different from what is reported in the western literature with more incidences in male sex and pediatric age group. Recurrences after surgery alone can be quite high(40% in our series). Positive margin & recurrent tumors were found to be adverse prognostic factor for recurrence in our series. Even in negative margin the recurrence rate was high this we believe is due to multicentricity of the lesion. Addition of radiation provides good local control but should be used with diligence as most of the recurrences are surgically salvageable and these tumors occur in young patients with long life expectancy. The role of systemic therapy including Tamoxifen needs further evaluation.

Aggressive fibromatosis is an enigma occupying the twilight zone between benign and malignant behavior. There are considerable lacunae in our knowledge regarding the natural course of the disease. Due to the rarity and slow growing nature of the disease there had not been many studies with adequate numbers and follow-up to optimize treatment protocol for this tumor. There had never been a randomized control study comparing different treatments undertaken anywhere in

the world. Multi institutional prospective randomized control trials may optimize the treatment protocol for this rare and enigmatic disease.

Bibliography

1. Alman BA, Pajerski ME, Diaz-Cano S, Corboy K, Wolfe HJ. Aggressive fibromatosis (desmoid tumor) is a monoclonal disorder. Diagn Mol Pathol 1997; 6:98 –101.

2. Wara WM, Phillips TL, Hill DR, et al. Desmoid tumors—treatment and prognosis. Radiology 1977; 124:225–226.

3. Li M, Cordon-Cardo C, Gerald WL, Rosai J. Desmoid fibromatosis is
a clonal process. Hum Pathol 1996; 27:939 –943.

4. Merchant NP, Lewis JJ, Leung DH, Woodruff JM, Brennan MF. Extremity and trunk desmoid tumors: a multifactorial analysis of outcome. Cancer (in press).

5. Wold LE, Weiland LH. Tumefactive fibro-inflammatory lesions of the
head and neck. Am J Surg Pathol 1983; 7:477– 482.

6. Exelby PR. Surgery of soft tissue sarcomas in children. Natl Cancer Inst Monogr 1981; 153–157.

7. Scott RJ, Taeschner W, Heinimann K, et al. Association of extracolonic manifestations of familial adenomatous polyposis with acetylation phenotype in a large FAP kindred. Eur J Hum Genet 1997; 5:43– 49.

8. Thomas JA, Kothare SN. Desmoid tumors of the abdominal wall. Indian J Cancer 1972; 9:66–69.

9. Rodriguez-Bigas MA, Mahoney MC, Karakousis CP, Petrelli NJ. Desmoid tumors in patients with familial adenomatous polyposis. Cancer 1994; 74:1270 –1274.

10. Penna C, Tiret E, Parc R, et al. Operation and abdominal desmoid tumors in familial adenomatous polyposis. Surg Gynecol Obstet 1993; 177:263–268.

11. Jones IT, Jagelman DG, Fazio VW, Lavery IC, Weakley FL, McGannon E. Desmoid tumors in familial polyposis coli. Ann Surg 1986;
204:94 –97.

12. Miralbell R, Suit HD, Mankin HJ, Zuckerberg LR, Stracher MA, Rosenberg AE. Fibromatoses: from postsurgical surveillance to combined
surgery and radiation therapy. Int J Radiat Oncol Biol Phys
1990; 18:535–540.

13. Posner MC, Shiu MH, Newsome JL, Hajdu SI, Gaynor JJ, Brennan MF. The desmoid tumor: not a benign disease. Arch Surg 1989;
124:191–196.

14. Pritchard DJ, Nascimento AG, Petersen IA. Local control of extraabdominal desmoid tumors. J Bone Joint Surg [Am] 1996; 78:848–
854.

15. Rock MG, Pritchard DJ, Reiman HM, Soule EH, Brewster RC. Extraabdominal desmoid tumors. J Bone Joint Surg [Am] 1984; 66:1369–
1374.

16. Anthony T, Rodriguez-Bigas MA, Weber TK, Petrelli NJ. Desmoid
tumors. J Am Coll Surg 1996; 182:369 –377.

17. Uzlov VA. On desmoid tumors of the abdominal wall. Khirurgiia (Mosk) 1968; 44:74 –77.

18. Baron RL, Lee JK. Mesenteric desmoid tumors: sonographic and computed-tomographic appearance. Radiology 1981; 140:777–779.

19. Radulescu D, Gavrilescu S, Budu S. Desmoid tumors of the abdominal wall. Rev Chir Oncol Radiol 1983; 32:407– 414.

20. Easter DW, Halasz NA. Recent trends in the management of desmoid
tumors. Summary of 19 cases and review of the literature. Ann Surg 1989; 210:765–769.

21. Leibel SA, Wara WM, Hill DR, et al. Desmoid tumors: local control
and patterns of relapse following radiation therapy. Int J Radiat Oncol Biol Phys 1983; 9:1167–1171.

22. Sherman NE, Romsdahl M, Evans H, Zagars G, Oswald MJ. Desmoid
tumors: a 20-year radiotherapy experience. Int J Radiat Oncol Biol Phys 1990; 19:37– 40.

23. Reitamo JJ, Scheinin TM, Hayry P. The desmoid syndrome. New aspects in the cause, pathogenesis and treatment of the desmoid tumor. Am J Surg 1986; 151:230 –237.

24. Kiel KD, Suit HD. Radiation therapy in the treatment of aggressive fibromatoses (desmoid tumors). Cancer 1984; 54:2051–2055.

25. Gunderson LL, Nagorney DM, McIlrath DC, et al. External beam and
intraoperative electron irradiation for locally advanced soft tissue sarcomas. Int J Radiat Oncol Biol Phys 1993; 25:647– 656.

26. Kinzbrunner B, Ritter S, Domingo J, Rosenthal CJ. Remission of rapidly growing desmoid tumors after tamoxifen therapy. Cancer 1983; 52:2201–2204.

27. Waddell WR. Treatment of intra-abdominal and abdominal wall desmoid tumors with drugs that affect the metabolism of cyclic 39,59-adenosine monophosphate. Ann Surg 1975; 181:299 –302.

28. Waddell WR, Kirsch WM. Testolactone, sulindac, warfarin, and vitamin K1 for unresectable desmoid tumors. Am J Surg 1991; 161:416–
421.

29. Harvey JC, Quan SH, Fortner JG. Gardner's syndrome complicated by mesenteric desmoid tumors. Surgery 1979; 85:475– 477.

30. Caldwell EH. Desmoid tumor: musculoaponeurotic fibrosis of the abdominal wall. Surgery 1976; 79:104 –106.

31. Lim CL, Walker MJ, Mehta RR, Das GT. Estrogen and antiestrogen
binding sites in desmoid tumors. Eur J Cancer Clin Oncol 1986; 22:583–587.

32. Fong Y, Rosen PP, Brennan MF. Multifocal desmoids. Surgery 1993;
114:902–906.

33. Waddell WR, Gerner RE, Reich MP. Nonsteroid antiinflammatory drugs and tamoxifen for desmoid tumors and carcinoma of the stomach.
J Surg Oncol 1983; 22:197–211.

34. Lanari A. Effect of progesterone on desmoid tumors (aggressive fibromatosis) [letter]. N Engl J Med 1983; 309:1523.

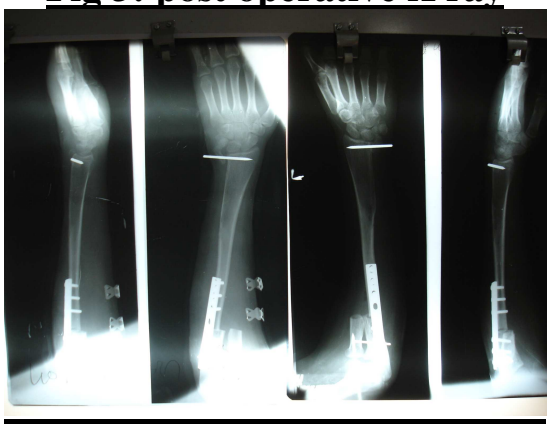
35. Wilcken N, Tattersall MH. Endocrine therapy for desmoid tumors. Cancer 1991; 68:1384 –1388.

Centralisation of ulna a unique limb salvage procedure

Fig 1: Preoperative photo

Fig 2: Defect after excision

Fig 3: post operative X ray



Scapulectomy

Fig 1: Pre operative photo

Fig 2: Intraoperative defect

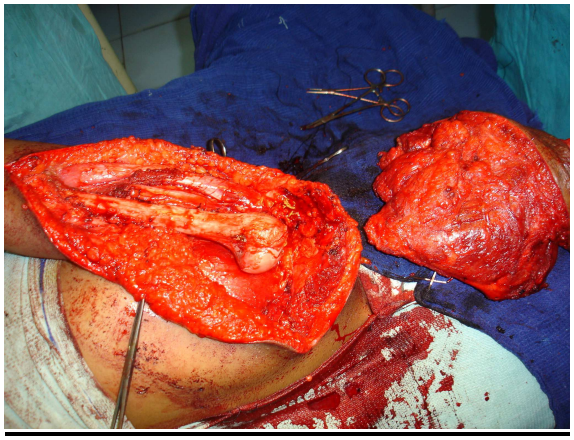


Fig 3: Post operative picture